

## PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference MM-V/PB60127		<b>FOR FURTHER ACTION</b>		See Form PCT/PEA/416
International application No. PCT/EP2004/007294		International filing date (day/month/year) 01.07.2004	Priority date (day/month/year) 04.07.2003	
International Patent Classification (IPC) or national classification and IPC C07D401/06, C08D487/04, A61K31/404, A61P29/00				
Applicant GLAXOSMITHKLINE S.P.A. et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (Indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand  03.05.2005		Date of completion of this report  30.06.2005		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Telephone No. +49 89 2399-8057 Stix-Malorny, E.		



**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/007294

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**Box No. I Basis of the report**

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1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

**Description, Pages**

1-70 as originally filed

**Claims, Numbers**

1-22 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
- \* If item 4 applies, some or all of these sheets may be marked "superseded."

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	1-22
	No: Claims	
Inventive step (IS)	Yes: Claims	1-22
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-22
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

## **V REASONED STATEMENT**

### **1. PRIOR ART**

The documents cited in the International Search Report

D1: GB-A-2 083 476 (WYETH JOHN & BROTHER LTD) 24 March 1982 (1982-03-24)

D2: WO 01/83454 A (GIARDINA GIUSEPPE ; GRUGNI MARIO (IT); RONZONI SILVANO (IT); BARLOCCO) 8 November 2001 (2001-11-08)

D3: WO 03/037863 A (SATTLEGGGER MICHAEL DR ; SCHICK HANS PROF DR (DE); ENLGBERGER WERNER DR) 8 May 2003 (2003-05-08)

have been considered for the examination procedure.

### **2. NOVELTY**

The subject-matter of the claims is considered to be novel (Article 33(2) PCT).

The compounds of claim 1 can be seen as a novel selection from D1 due to the substituted indole moiety. The compounds of D1 differ from claim 21 in the medical use.

Presently claimed compounds differ from D2 in the indole moiety, from D3 in the substitution of the piperidine moiety.

### **3. INVENTIVE STEP**

The subject-matter of the claims fulfil the requirements of Article 33(3) PCT for the following reasons:

The problem of the present application may be seen in the provision of further piperidine-substituted indoles possessing antagonistic or agonistic activity for the receptors ORL-1 and that are useful in treating disorders related to modulation of these receptors, e.g. pain.

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(SEPARATE SHEET)**

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The closest state of the art for the present application is represented by D2. D2 discloses structurally similar compounds exhibiting the same pharmaceutical activity. As already stated above the compounds differ in the indole unity. The compounds of D3 are useful in a similar field and differ in an other manner as explained above.

Neither through combination of the said documents nor through variation within said documents the skilled person would arrive at the presently claimed solution. Accordingly the solution to the problem defined above does not appear to be evident.

It is derivable from the description that the applicant has carried out tests that proof the alleged activity.

Thus, inventive step can be acknowledged.

In the regional phase it might become necessary to name at least one exemplified compound for which a test has been carried out in order to assess the plausibility of the generalisation and the scope of the claims.